A randomized controlled study evaluating the effectiveness of a two-step self-etch adhesive with and without selective phosphoric-acid etching of enamel

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Summary  Objectives: The purpose of this randomized controlled clinical trial was to test the hypothesis that a two-step self-etch approach is equally effective to restore cervical class-V lesions as a self-etch approach with beforehand selective etching of enamel using phosphoric acid.

Methods: Twenty-nine patients received two or four restorations randomly following two experimental protocols ('paired-tooth' study design): (1) A 'mild' self-etch adhesive (Clearfil SE, Kuraray) was applied following a self-etch approach on both enamel and dentin (C-SE non-etch); (2) Similar application of Clearfil SE, but including beforehand selective acid-etching of the enamel cavity margins with 40% phosphoric acid (C-SE etch). Clearfil AP-X (Kuraray) was used as restorative composite for all 100 restorations. The clinical effectiveness was recorded in terms of retention, marginal integrity and clinical micro-leakage after 2 years of clinical service.

Results: No restoration losses were recorded. Clinical micro-leakage was slight and only rarely observed. No significant differences were found between both groups for the diverse parameters evaluated except for the number of small incisal marginal defects, which was significantly higher in the C-SE non-etch group (McNemar: $p=0.0391$).

Significance: The clinical effectiveness of the mild two-step self-etch adhesive Clearfil SE was excellent after 2 years of clinical service. Although in general no difference in clinical performance was recorded when Clearfil SE was applied following either of the experimental protocols, more marginal defects at the enamel
Introduction

Today’s adhesives are applied following either an ‘etch and rinse’ or ‘self-etch’ approach [1]. Clinical trials have documented that reliable and relatively long-lasting adhesive restorations can be achieved using etch and rinse adhesives [2–9]. Clinical trials investigating the effectiveness of self-etch adhesives is, however, limited [10–13]. Self-etch adhesives nevertheless possess the clinical advantage that no intermediary rinse step is needed, making them more user-friendly and less technique-sensitive. Furthermore, as self-etching does not open the dentin tubules, but rather dissolves/infiltrates the tubule smear plug (in contrast to an etch&rinse approach that widely opens tubules), self-etch adhesives have been reported to induce significantly less post-operative sensitivity [11,14–17]. Among current self-etch adhesives, one- and two-step adhesives exist that depending on their acidity belong either to so-called ‘mild’ or ‘strong’ self-etch adhesives [1]. So far, a two-step application procedure outperforms the single-step procedure, as corroborated by many laboratory studies [1,18–23]. While a strong self-etch approach appears more favorable when bonding to enamel [1], a mild self-etch procedure that leaves hydroxyapatite within a submicron hybrid layer available for additional chemical interaction, warrants better bonding to dentin [1,24].

Most concern remains regarding the enamel etching-capability of the relatively high-pH mild self-etch adhesives. Often in daily clinical practice, they are applied after first having selectively etched the enamel cavity margins with conventional 30–40% phosphoric acid. Indeed, mild self-etch adhesives demineralize enamel less effectively than conventional phosphoric acid-etchants that need to be rinsed off [25]. The literature is equivocal on this issue. Some studies have reported that self-etch adhesives bond less effectively to enamel than total-etch or etch&rinse systems that use phosphoric acid [26–29]. Other studies have reported that both self-etch and etch&rinse adhesives perform equally well on ground enamel [25,30–34]. Though the enamel-etch pattern resulting from a mild self-etch adhesive is less defined when compared to that resulting from phosphoric-acid etching [35], no correlation was found between enamel-etch morphology and shear bond strength to ground enamel [36].

Mild self-etch adhesives have also been reported to less effectively interact with dentin, in particular when prepared by a coarse-grit diamond that resulted in a rather compact, thick and thus relatively difficult to penetrate smear layer [37–40]. In addition, with regard to bond durability, bonds produced by self-etch adhesives appear more vulnerable to degradation due to areas of increased permeability present at the hybridized adhesive-dentin interface complex [41]. Water was suggested to be incompletely removed and resulted in regions of incomplete polymerization and/or hydrogel formation, making the interface permeable and thus more degradation sensitive.

Though new in-vitro testing methodology tends to better predict clinical performance [1,42,43], clinical trials remain needed to ultimately evaluate the clinical efficacy of such self-etch adhesives. To date, clinical trials evaluating adhesives are, however, rather scarce, the main reason for which is that manufacturers often introduce a successor product to the market even before a trial on the precursor product has been completed. Another problem of clinical trials is the many clinical variables simultaneously involved [8,44], making clear interpretations regarding clinical effectiveness of the adhesive itself often difficult or even not justified. The objective of this article is to report the 2-year results of a randomized controlled clinical trial investigating the clinical effectiveness of a representative mild two-step self-etch adhesive following a ‘paired-tooth’ study design. The actual hypothesis tested was that a two-step self-etch approach is equally effective to restore cervical class-V lesions as a self-etch approach with beforehand selective etching of enamel using phosphoric acid.

Materials and methods

The clinical effectiveness of Clearfil SE (Kuraray, Tokyo, Japan), representing the group of mild self-etch adhesives [1], was evaluated when applied strictly following a self-etch approach on both enamel and dentin (according to manufacturer’s instructions; abbreviated as ‘C-SE
non-etch’) and compared to the application of the same adhesive following the same application protocol, but after the enamel cavity margins were selectively acid-etched with 40% phosphoric acid (control; abbreviated as C-SE etch).

**Inclusion and exclusion criteria**

Twenty-nine subjects (ranging in age from 36 to 75 years) were enrolled in the study. They were all non-hospitalized patients recruited from the university hospital that were in need of cervical restorations. Patients with compromised medical history, severe or chronic periodontitis, extreme caries sensitivity and heavy bruxism were excluded from the study. Prior to participating in the study all patients signed a written consent. The clinical trial protocol was approved by the Commission for Medical Ethics of the Catholic University of Leuven. Fifty pairs of equal teeth (first and second premolar at the same side, left and corresponding right incisor, canine or premolar, respectively,) were restored. A pre-set table mentioning 50 pairs of an experimental and control treatment protocol in random order was used to assign the treatment protocol to each tooth. The tooth with the highest tooth number received the treatment mentioned first, while the one with the lowest number received the treatment mentioned second. All restorations were placed in cervical non-carious erosion/abrasion/abfraction lesions. Prior to restoration, the lesions were categorized in terms of shape (wedge-sharp versus saucer-rounded), depth ($\leq 1$ mm or $>1$ mm), cervico-incisal size ($<1.5$ mm, $1.5-2.5$ mm, $>2.5$ mm), degree of dentin sclerosis (none, slight, moderate, severe) and presence of attrition facets on the incisal edge or occlusal cusp. Maximum two pairs of restorations were placed in one patient. The two treatment protocols were mutually compared per restoration pair.

**Restorative procedure**

Operative procedures were performed by two specially instructed and experienced dentists from the university dental school. If needed to prevent patient discomfort during restorative procedures, local anesthesia was applied with 1.8 ml of 2% lidocain with 1:80,000 epinephrine (Lignospan 2%, Septodont, St-Maur, France). All restorative procedures were done under rubber-dam isolation using the gingival retraction clamp Ivory212 (Columbus Dental, St Louis, MO, USA). The tooth surface was first cleansed with a slurry of pumice and water to remove the salivary pellicle and any remaining dental plaque. The dentin walls of the lesion were superficially roughened with a coarse diamond bur to remove any superficial caries or discolored tooth tissue before the bonding procedure was initiated. Tooth preparation did include a 1-2 mm short enamel bevel to increase surface area for bonding and to enhance aesthetics. No lining material was applied. Lesions were restored according to the manufacturer’s instructions (Table 1) except for the control group, when the enamel margins were beforehand selectively etched with 40% phosphoric acid (K-etchant, Kuraray) during 15 s and subsequently thoroughly rinsed, and air-dried. The natural cervical tooth anatomy was restored with Clearfil AP-X (Kuraray) in minimally two increments to reduce polymerization shrinkage effects and to achieve effective setting upon curing using an Optilux 500 light-curing unit (Demetron-Kerr) with a light output not less than 550 mW/cm². Finishing and polishing were accomplished using pinetree-shaped contouring diamonds (Komet, Lemgo, Germany), rubber points (Eve, Ernst Vetter, Pforzhein, Germany), flexible discs and finishing strips (Sof-Lex Pop-On set, 3M, St Paul, MN, USA).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Adhesive composition and application procedure.</th>
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<tr>
<td>Adhesive</td>
<td>Components and composition</td>
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<tr>
<td>Clearfil SE (Kuraray, Tokyo, Japan)</td>
<td>Primer: 10-MDP, HEMA, hydrophilic dimethacrylate, CQ, N,N-diethanol p-toludine, water</td>
</tr>
<tr>
<td></td>
<td>Adhesive: 10-MDP, Bis-GMA, HEMA, hydrophilic dimethacrylate, CQ, N,N-diethanol p-toludine, silanized colloidal silica</td>
</tr>
<tr>
<td>K-etchant (Kuraray)</td>
<td>40% phosphoric acid, thickener</td>
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Bis-GMA, bisphenol-glycidyl methacrylate; CQ, dl-camphorquinone; HEMA, hydroxyethyl methacrylate; 10-MDP, 10-methacryloyloxydecyl dihydrogen phosphate.
Evaluation criteria and procedure

Restorations were examined at baseline, 6 months, 1 year and 2 years of clinical service for retention, marginal integrity, clinical micro-leakage, post-operative sensitivity, caries recurrence, and tooth vitality. All parameters were recorded using a modified index system introduced by Vanherle et al. [45]. Color slides were made pre-operatively, at baseline and at each recall. Two independent examiners carried out all evaluations using the predetermined set of criteria [45]. The evaluators were blinded to the adhesive technique used in any given restoration. Any discrepancy between evaluators was resolved at chair side. Clinical effectiveness was determined in terms of the abovementioned parameters, of which retention (no complete loss of restoration), marginal integrity (severe defects) and clinical micro-leakage (severe discoloration) were considered as key parameters, determining the overall parameter ‘clinical success rate’.

Statistical analysis

Statistical analysis compared on a pair-wise basis the ratings of retention, perfect marginal integrity and absence of clinical micro-leakage between the experimental and control group using the McNemar test at a significance level of 5% ($p < 0.05$).

Results

The clinical data for the diverse parameters evaluated are summarized in Table 2. Major parameters such as retention rate, perfect marginal integrity, absence of clinical micro-leakage, absence of sensitivity, absence of caries recurrence, preservation of tooth vitality and the overall clinical success rate are depicted as a function of time for the experimental and control group in the Fig. 1. The recall rate was 86% or higher at the different recalls for both experimental groups. Reasons for not showing up at each recall were checked. They appeared not related to any negative appreciation of the patient for the restorative work done (nor to lost restorations), but rather because of secondary reasons such as crown restoration of teeth involved (four restorations in one patient at the 1- and 2-year recall, or 4% of the total restoration number), the patient that moved to an area away from Leuven (two restorations in one patient at the 2-year recall, or 2%), or the patient that could not be reached
because of unknown reasons (eight restorations in two patients at the 2-year recall, or 8%).

None of the restorations was lost during the 2-year study period resulting in an excellent 100% retention rate for both the experimental C-SE non-etch as the control C-SE etch group. With regard to marginal integrity, statistical analysis revealed significant differences between the two groups only at the 2-year control (Table 3). Additional selective etching of enamel margins with phosphoric acid (C-SE etch) resulted in a significantly higher percentage of ‘perfect marginal integrity’ than when the adhesive was applied following a solely self-etch approach (C-SE non-etch). At all recalls, the C-SE non-etch group revealed more ‘enamel margin defects’ than C-SE etch group, of which the difference became statistically significant at the 2-year recall. Regarding ‘dentin margin defects’, some variation in occurrence was observed with the C-SE etch group having a higher percentage of dentin margin defects than the C-SE non-etch group at the 6-month and 1-year recall, and vice versa at the 2-year recall. None of these differences were statistically significant. All margin defects, either recorded along the enamel or dentin margins, were recorded as ‘small’. No severe enamel or dentin margin defects were recorded for both groups up to the 2-year recall.

With regard to clinical micro-leakage, only 7 and 5%, respectively, of the C-SE non-etch and C-SE etch restorations demonstrated superficial, localized margin discoloration. For both groups, no

![Figure 1](image)

Figure 1 Graph presenting the results of the major evaluation criteria in function of time for the experimental C-SE non-etch and the control C-SE etch group.

### Table 3 McNemar pair-wise statistical analysis.

<table>
<thead>
<tr>
<th>C-SE non-etch</th>
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<tr>
<td>6-Month recall</td>
<td>1-Year recall</td>
</tr>
<tr>
<td>Fail No fail</td>
<td>Fail No fail</td>
</tr>
<tr>
<td>Perfect marginal integrity</td>
<td>&gt;0.9999</td>
</tr>
<tr>
<td>Enamel margin defects</td>
<td>&gt;0.9999</td>
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</tr>
</tbody>
</table>

\[a\] Recall rate = 100% (100 out of 100 restorations examined).

\[b\] Recall rate = 96% (96 out of 100 restorations examined).

\[c\] Recall rate = 86% (86 out of 100 restorations examined).
Discussion

Non-carious mixed enamel/dentin class-V lesions were selected to test the clinical effectiveness of the two-step self-etch adhesive Clearfil SE in this study. Cervical lesions are regarded as the ideal cavities to test the clinical effectiveness of adhesives because (1) they present no macro-mechanical undercuts; (2) they require for at least 50% bonding to dentin; (3) when restored, they result in an enamel as well as dentin margin; (4) they are widely available; (5) they are usually found in anterior teeth or premolars with good access and (6) they have the worst long-term prognosis because of the high proportion of dentin margins and the high stress build-up in the cervical area [1,8,46]. This clinical trial was randomized and the examiners were blinded for the adhesive approach applied per lesion and per patient. The paired-tooth design involved the placement of two or four of the two adhesive/composite protocols per patient, and this in pairs of equal teeth (first and second premolar at the same side, left and corresponding right incisor, canine or premolar, respectively). Consequently, clinical effectiveness was pair-wise evaluated at the patient level, comparing both adhesive protocols mutually for each pair. Clearfil SE (combined with Clearfil AP-X) was chosen representing so-called mild two-step self-etch adhesives because of its repeatedly proven excellent performance in independent laboratory studies [1,9,18,21,23,32,34,35]. As control, Clearfil SE was applied on enamel/dentin in the same manner with the only difference that the enamel cavity margins were selectively etched using 40% phosphoric acid prior to the application of Clearfil SE. The rationale behind this study design was that following laboratory findings an etch&rinse approach (including phosphoric-acid etching) still provides the most effective bond to enamel, while not much difference in bonding effectiveness to dentin was found between an etch&rinse and a mild self-etch approach [1].

This randomized controlled clinical trial revealed that up to 2 years of clinical service the mild two-step self-etch adhesive Clearfil SE (Kuraray) performed excellent (C-SE non-etch). With regard to the primary evaluation parameters that determine the ‘overall clinical success’ rate, no significant difference was recorded with the control group (C-SE etch). The only parameter that appeared significantly different between both groups is the higher prevalence of small enamel margin defects recorded when Clearfil SE was applied following a solely self-etch approach (Tables 2 and 3). It should, however, be emphasized that these defects are small in a sense that they can hardly be spotted by the naked eye, but can only be sensed by moving a relatively sharp probe under light pressure across the restoration-tooth margin. These defects did certainly not require any repair (nor replacement of the whole restoration), and therefore should be regarded as being of clinically negligible relevance.

Clearfil SE is a two-step self-etch adhesive, of which the self-etching primer contains 10-methacyloxydecyl dihydrogen phosphate (10-MDP) as functional monomer dissolved in water to result in a pH of around 2 (Table 1). Clearfil SE interacts with dentin rather superficially producing a hybrid layer of about 1 μm depth at maximum. The excellent clinical effectiveness of Clearfil SE recorded in this study may therefore in part result from simultaneous demineralization and infiltration of dentin, having lead to a shallow, but uniform and thus stable resin-infiltrated dentin layer [14,39]. Furthermore, within the shallow hybrid layer residual hydroxyapatite around the exposed collagen fibrils remains available for additional chemical interaction with the functional monomer 10-MDP [1,24,47]. Following recent research, 10-MDP has been shown to chemically interact with hydroxyapatite [24]. Among three monomers investigated (10-MDP, 4-MET or 4-methacyloxyethyl trimellitic acid, and phenyl-P or 2-methacyloxyethyl phenyl hydrogen phosphate), 10-MDP revealed not only the most intense chemical interaction with hydroxyapatite, but the resultant bond with calcium appeared also most hydrolytically stable [24]. Besides self-etching, such an additional chemical bonding efficacy of 10-MDP with tooth minerals should theoretically contribute to the actual adhesive potential to dentin, but also to enamel that consists of nearly only mineral substance, with which 10-MDP can chemically react. The resulting two-fold micro-mechanical and chemical bonding mechanism may
thus to a large extent have lead to the excellent clinical performance of Clearfil SE recorded in this study. It may also explain why despite the rather mild enamel-etching effect (as compared to that resulting from phosphoric-acid etching), Clearfil SE bonded fairly well to enamel (no severe margin defects). Actually, the examiners could never tell which of the two restorations (per pair) was placed following a full self-etch application protocol, or following a self-etch procedure after enamel was selectively etched with phosphoric acid. Besides preventing restoration loss, such intimate mono-
mer-tooth tissue interaction may also better pro-
tect the restoration against marginal leakage over
mer–tooth tissue interaction may also better pro-
tect the restoration against marginal leakage over
time [48,49]. This was confirmed in this study, in
which hardly any marginal discoloration as clinical
sign of leakage was recorded, and this irrespective
of if Clearfil SE was applied following the exper-
imental or control application protocol (Table 2 and
Fig. 1).

The retention as well as the clinical micro-
leakage rates of Clearfil SE applied following either
of the two adhesive approaches exceeded by far the
ADA guidelines (less than 10% restoration loss and
depth restoration staining at 18 months) to acquire
‘full acceptance’ [50]. Consequently, up to 2 years
of clinical service the two-step self-etch approach
was equally effective to restore cervical class-V
lesions as the control approach that received
beforehand selective etching of enamel with phosphoric acid, by which the hypothesis advanced
in this study was rejected.

Another factor that may have contributed to the
excellent clinical performance of Clearfil SE is the
particle-filled adhesive resin that has a filler
content of 10 wt%. Clearfil SE contains nano-filler
(20 nm, according to technical information pro-
vided by Kuraray), resulting in a thicker adhesive
layer and thus more flexible interface that is
thought to relieve interfacial tensile stress (stress-
absorber) between the shrinking composite and the
rigid dentin substrate [51–53]. Such a flexible
intermediary resin may also help to counteract
other stress factors (like occlusal loading) that must
affect the bond longevity over time.

When compared to the clinical performance of
other adhesives, Clearfil SE as a two-step self-etch
adhesive performs up to 2 years as favorable as
conventional three-step etch&rinse adhesives [1,3,
4,6–8]. An apparently less favorable clinical effec-
tiveness of Clearfil SE with a 2-year retention rate
of 93% was reported by Türkün [13]. Unfortunately,
the actual number of restoration losses was not
mentioned in that paper, since the author clearly
stated that four non-recalled patients (with one to
possibly three restorations) ‘were considered to
have missing restorations’ [13]. Consequently, the
actual retention rate should have been substan-
tially higher than the reported 93% (when the non-
recalled restorations would not have been taken in
consideration). In literature, no other clinical trial
was found to have tested the clinical effectiveness
of Clearfil SE in cervical lesions. Some clinical data
are available on its predecessor Clearfil Liner Bond
2 (Kuraray) that also belongs to the group of mild
two-step self-etch adhesives [1]. A 91% 2-year and a
92% 3-year retention rate were reported, respect-
ively, by van Dijken [54] and Latta et al [55]. The
two-step self-etch adhesive Clearfil Liner Bond 2
and its successor Clearfil SE differ for the functional
monomer, with phenyl-P in Clearfil Liner Bond 2
being replaced by the more stable 10-MDP monomer
in its successor Clearfil SE. One may consequently
expect that Clearfil SE performs clinically better
than its predecessor, as confirmed in this study with
a 100% retention rate at 2 years. Much less
favorable clinical effectiveness is commonly
recorded for other simplified two-step etch&rinse
[3,4,56–60] and one-step self-etch adhesives
[10,54,58,61].

Patients that received Clearfil SE restorations
reported hardly any post-operative sensitivity. This
indicates that dentin tubules as the direct connec-
tion to the pulp must have been adequately sealed
by the two-step self-etch approach, thereby con-
firming the claim often made that self-etch
adhesives better prevent post-operative sensitivity.
Remaining evaluation criteria, such as caries
recurrence, aesthetics, gingival response, tooth
vitality and post-operative sensitivity were all rated
satisfactory. Other clinical co-variables that have
been described to affect adhesion to tooth tissue
include patient age, dentin sclerosis, lesion size and
shape, tooth type, enamel and dentin structure,
tooth location and stressful occlusion, among other
[8,44]. The clinical failure rates in this study were
so low that no correlation could be made with these
co-variables.

Conclusion

The clinical effectiveness of the mild two-step self-
etch adhesive Clearfil SE was excellent after 2 years
of clinical service. Although in general no differ-
ce in clinical performance was recorded when
Clearfil SE was applied following either the exper-
imental or control protocol, more marginal defects
at the enamel side were noticed when enamel was
not beforehand etched with phosphoric acid. How-
ever, these defects were small and of clinical
negligible relevance. Long-term recalls are planned to find out if difference in clinical performance between the experimental and control group will occur at later restoration ages.

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